WO 2004/058182 PCT/US2003/041229

We claim:

1. A method of treating or preventing bacterial infections, comprising administering to a subject in need of such therapy a therapeutically effective amount of a synergistic combination of:

- (a) at least two bacteriophage derived lytic enzymes; and
- (b) a suitable carrier for delivery of the lytic enzymes to the site of infection.
- 2. The method of claim 1, wherein said at least two bacteriophage derived lytic enzymes are selected from the group consisting of an amidase, a muramidase, an endopeptidase, a glucosaminidase and combinations thereof.
- 3. The method of claim 1, wherein said at least two bacteriophage derived lytic enzymes are an amidase and a muramidase.
- 4. The method of claim 3, wherein the muramidase is lysozyme.
- 5. The method of claim 4, wherein the lysozyme is Cpl-1.
- 6. The method of claim 1, wherein the lytic enzymes are selected from the group consisting of Pal and Cpl-1.
- 7. The method of claim 1, wherein the bacterial infections are caused by Streptococcus pneumoniae.
- 8. The method of claim 1, wherein the lytic enzymes decrease the occurrence or severity of local and systemic pneumococcal disease.
- 9. The method of claim 1, wherein the lytic enzymes prevent or eliminate pneumococcal colonization.

37

10. The method of claim 1, wherein said at least two lytic enzymes are isolated from the phage of disease causing bacteria, and wherein said disease causing bacteria are gram positive bacteria.

WO 2004/058182 PCT/US2003/041229

11. A method of treating or preventing bacterial infections, comprising administering to a subject in need of such therapy a therapeutically effective amount of bacteriophage derived lytic enzymes selected from the group consisting of an amidase, a muramidase, an endopeptidase, a glucosaminidase, and synergistic combinations thereof.

- 12. The method of claim 10, wherein the gram positive bacteria is Streptococcus.
- 13. The method of claim 12, wherein the Streptococcus is Streptococcus pneumoniae.
- 14. The method of claim 11, wherein the amidase is Pal and the muramidase is Cpl-1.
- 15 A pharmaceutical composition comprising:
 - (a) at least two therapeutically effective synergistic bacteriophage derived lytic enzymes; and
 - (b) a carrier suitable for delivery of the lytic enzymes to the site of infection.
- 16. The composition of claim 15, wherein said at least two bacteriophage derived lytic enzymes are selected from the group consisting of an amidase, a muramidase, an endopeptidase, a glucosaminidase and combinations thereof.
- 17. The pharmaceutical composition of claim 16, wherein the amidase is Pal and the muramidase is Cpl-1.
- 18. A screening method for identifying agents capable of enhancing the activity of Pal and Cpl-1, comprising:
 - (a) preparing purified Pal and Cpl-1;
- (b) contacting the Pal and Cpl-1 to a bacteria having radioactively labeled peptidoglycan in the cell wall in the presence or absence of a test compound under conditions which allow binding to the peptidoglycan; and
- (c) determining the amount of peptidoglycan cleavage, wherein an agent capable of enhancing Pal and Cpl-1 activity is identified when the release of radioactivity is enhanced in the presence but not the absence of the agent.

WO 2004/058182 PCT/US2003/041229

19. An anti-microbial composition for sanitizing or decontaminating porous or non-porous surfaces comprising at least two bacteriophage derived synergistic lytic enzymes.

- 20. The composition of claim 19, wherein said at least two bacteriophage derived synergistic lytic enzymes are selected from the group consisting of an amidase, a muramidase, an endopeptidase, a glucosaminidase and combinations thereof.
- 21. The composition of claim 19, wherein said at least two bacteriophage derived lytic enzymes are an amidase and a muramidase.
- 22. The composition of claim 21, wherein the muramidase is lysozyme.
- 23. The composition of claim 22, wherein the lysozyme is Cpl-1.
- 24. A method for decontaminating inanimate surfaces suspected of containing infectious bacteria comprising treatment of said surfaces with a bacteriocidal or bacteriostatically effective amount of the composition of claim 19.
- 25. Use of at least two therapeutically effective synergistic bacteriophage derived lytic enzymes for the preparation of a composition for the treatment of bacterial infections.
- 26. Use according to claim 25, whrein the lytic enzymes are selected from the group consisting of an amidase, a muramidase, an endopeptidase, a glucosaminidase, and combinations thereof.
- 27. Use according to claim 26, wherein the muramidase is lysozyme.
- 28. Use according to claim 27, wherein the lysozyme is Cpl-1.
- 29. Use according to claim 26, wherein the amidase is Pal.